



## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use VENOFR® safely and effectively. See full prescribing information for VENOFR.

**Venofer (iron sucrose) injection, for intravenous use**  
Initial U.S. Approval: 2000

### INDICATIONS AND USAGE

Venofer is an iron replacement product indicated for the treatment of iron deficiency anemia (IDA) in patients with chronic kidney disease (CKD). (1)

### DOSAGE AND ADMINISTRATION

Population		Dose
Adult patients	Hemodialysis Dependent-Chronic Kidney Disease (HDD-CKD) (2.2)	100 mg slow intravenous injection or infusion
	Non-Dialysis Dependent-Chronic Kidney Disease (NDD-CKD) (2.3)	200 mg slow intravenous injection or infusion
	Peritoneal Dialysis Dependent-Chronic Kidney Disease (PDD-CKD) (2.4)	300 mg or 400 mg intravenous infusion
Pediatric patients	HDD-CKD (2.5), PDD-CKD or NDD-CKD (2.6)	0.5 mg/kg slow intravenous injection or infusion

### DOSAGE FORMS AND STRENGTHS

Injection: 50 mg/2.5 mL, 100 mg/5 mL, or 200 mg/10 mL (20 mg/mL) in single-dose vials. (3)

### CONTRAINDICATIONS

- Known hypersensitivity to Venofer. (4)

### WARNINGS AND PRECAUTIONS

- Hypersensitivity Reactions: Observe for signs and symptoms of hypersensitivity during and after Venofer administration for at least 30 minutes and until clinically stable following completion of each administration. Only administer Venofer when personnel and therapies are immediately available for the treatment of serious hypersensitivity reactions. (5.1)
- Hypotension: May cause hypotension. Monitor for signs and symptoms of hypotension during and following each administration. (5.2)
- Iron Overload: Regularly monitor hematologic responses during therapy. Do not administer to patients with iron overload. (5.3)

### ADVERSE REACTIONS

- Adult patients: The most common adverse reactions (≥2%) are diarrhea, nausea, vomiting, headache, dizziness, hypotension, pruritus, pain in extremity, arthralgia, back pain, muscle cramp, injection site reactions, chest pain, and peripheral edema. (6.1)
- Pediatric patients: The most common adverse reactions (≥2%) are headache, respiratory tract viral infection, peritonitis, vomiting, pyrexia, dizziness, cough, nausea, arteriovenous fistula thrombosis, hypotension, and hypertension. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact American Regent, Inc. at 1-800-734-9236 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Venofer is indicated for the treatment of iron deficiency anemia (IDA) in patients with chronic kidney disease (CKD).

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Mode of Administration

Administer Venofer only intravenously by slow injection or by infusion. The dosage of Venofer is expressed in mg of elemental iron. Each mL contains 20 mg of elemental iron.

#### 2.2 Adult Patients with Hemodialysis Dependent-Chronic Kidney Disease (HDD-CKD)

Administer Venofer 100 mg undiluted as a slow intravenous injection over 2 to 5 minutes, or as an infusion of 100 mg diluted in a maximum of 100 mL of 0.9% NaCl over a period of at least 15 minutes, per consecutive hemodialysis session [see *How Supplied/Storage and Handling* (16.2)]. Administer Venofer early during the dialysis session (generally within the first hour). The usual total treatment course of Venofer is 1000 mg. Venofer treatment may be repeated if iron deficiency recurs.

#### 2.3 Adult Patients with Non-Dialysis Dependent-Chronic Kidney Disease (NDD-CKD)

Administer Venofer 200 mg undiluted as a slow intravenous injection over 2 to 5 minutes or as an infusion of 200 mg in a maximum of 100 mL of 0.9% NaCl over a period of 15 minutes. Administer on 5 different occasions over a 14 day period. There is limited experience with administration of an infusion of 500 mg of Venofer, diluted in a maximum of 250 mL of 0.9% NaCl, over a period of 3.5 to 4 hours on Day 1 and Day 14 [see *How Supplied/Storage and Handling* (16.2)]. Venofer treatment may be repeated if iron deficiency recurs.

#### 2.4 Adult Patients with Peritoneal Dialysis Dependent-Chronic Kidney Disease (PDD-CKD)

Administer Venofer in 3 divided doses, given by slow intravenous infusion, within a 28 day period: 2 infusions each of 300 mg over 1.5 hours 14 days apart followed by one 400 mg infusion over 2.5 hours 14 days later. Dilute Venofer in a maximum of 250 mL of 0.9% NaCl [see *How Supplied/Storage and Handling* (16.2)]. Venofer treatment may be repeated if iron deficiency recurs.

#### 2.5 Pediatric Patients (2 Years of Age and Older) with HDD-CKD for Iron Maintenance Treatment

For iron maintenance treatment: Administer Venofer at a dose of 0.5 mg/kg, not to exceed 100 mg per dose, every two weeks for 12 weeks given undiluted by slow intravenous injection over 5 minutes or diluted in 0.9% NaCl at a concentration of 1 to 2 mg/mL and administered over 5 to 60 minutes. Do not dilute to concentrations below 1 mg/mL [see *How Supplied/Storage and Handling* (16.2)]. Venofer treatment may be repeated if necessary.

The dosing for iron replacement treatment in pediatric patients with HDD-CKD has not been established.

#### 2.6 Pediatric Patients (2 Years of Age and Older) with NDD-CKD or PDD-CKD who are on Erythropoietin Therapy for Iron Maintenance Treatment

For iron maintenance treatment: Administer Venofer at a dose of 0.5 mg/kg, not to exceed 100 mg per dose, every four weeks for 12 weeks given undiluted by slow intravenous injection over 5 minutes or diluted in 0.9% NaCl at a concentration of 1 to 2 mg/mL and administered over 5 to 60 minutes. Do not dilute to concentrations below 1 mg/mL [see *How Supplied/Storage and Handling* (16.2)]. Venofer treatment may be repeated if necessary.

The dosing for iron replacement treatment in pediatric patients with NDD-CKD or PDD-CKD has not been established.

### 3 DOSAGE FORMS AND STRENGTHS

Injection: 50 mg/2.5 mL, 100 mg/5 mL, or 200 mg/10 mL (20 mg/mL) in single-dose vials.

### 4 CONTRAINDICATIONS

- Known hypersensitivity to Venofer.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylactic-type reactions, some of which have been life-threatening and fatal, have been reported in patients receiving Venofer. Patients may present with shock, clinically significant hypotension, loss of consciousness, and/or collapse. If hypersensitivity reactions or signs of intolerance occur during administration, stop Venofer immediately. Monitor patients for signs and symptoms of hypersensitivity during and after Venofer administration for at least 30 minutes and until clinically stable following completion of the infusion. Only administer Venofer when personnel and therapies are immediately available for the treatment of serious hypersensitivity reactions. Most reactions associated with intravenous iron preparations occur within 30 minutes of the completion of the infusion [see *Adverse Reactions* (6.1 and 6.2)].

#### 5.2 Hypotension

Venofer may cause clinically significant hypotension. Monitor for signs and symptoms of hypotension following each administration of Venofer. Hypotension following administration of Venofer may be related to the rate of administration and/or total dose administered [see *Dosage and Administration* (2), *Warnings and Precautions* (5.1), and *Adverse Reactions* (6.2)].

#### 5.3 Iron Overload

Excessive therapy with parenteral iron can lead to excess storage of iron with the possibility of iatrogenic hemosiderosis. All adult and pediatric patients receiving Venofer require periodic monitoring of hematologic and iron parameters (hemoglobin, hematocrit, serum ferritin and transferrin saturation). Do not administer Venofer to patients with evidence of iron overload. Transferrin saturation (TSAT) values increase rapidly after intravenous administration of iron sucrose; do not perform serum iron measurements for at least 48 hours after intravenous dosing [see *Dosage and Administration* (2) and *Overdosage* (10)].

### 6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypersensitivity Reactions [see *Warnings and Precautions* (5.1)]
- Hypotension [see *Warnings and Precautions* (5.2)]
- Iron Overload [see *Warnings and Precautions* (5.3)]

#### 6.1 Adverse Reactions in Clinical Trials

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug may not reflect the rates observed in practice.

##### Adverse Reactions in Adult Patients with CKD

The frequency of adverse reactions associated with the use of Venofer has been documented in six clinical trials involving 231 patients with HDD-CKD, 139 patients with NDD-CKD and 75 patients with PDD-CKD. Adverse reactions reported by ≥ 2% of treated patients in the six clinical trials for which the rate for Venofer exceeds the rate for comparator are listed by indication in Table 1. Patients with HDD-CKD received 100 mg doses at 10 consecutive dialysis sessions until a cumulative dose of 1000 mg was administered. Patients with NDD-CKD received either 5 doses of 200 mg over 2 weeks or 2 doses of 500 mg separated by fourteen days, and patients with PDD-CKD received 2 doses of 300 mg followed by a dose of 400 mg over a period of 4 weeks.

Table 1. Adverse Reactions Reported in ≥ 2% of Study Populations and for which the Rate for Venofer Exceeds the Rate for Comparator

Body System/Adverse Reactions	HDD-CKD	NDD-CKD		PDD-CKD	
	Venofer (N=231) %	Venofer (N=139) %	Oral Iron (N=139) %	Venofer (N=75) %	EPO* Only (N=46) %
<b>Subjects with any adverse reaction</b>	78.8	76.3	73.4	72.0	65.2
<b>Ear and Labyrinth Disorders</b>					
Ear Pain	0	2.2	0.7	0	0
<b>Eye Disorders</b>					
Conjunctivitis	0.4	0	0	2.7	0
<b>Gastrointestinal Disorders</b>					
Abdominal pain	3.5	1.4	2.9	4.0	6.5
Diarrhea	5.2	7.2	10.1	8.0	4.3
Dysgeusia	0.9	7.9	0	0	0
Nausea	14.7	8.6	12.2	5.3	4.3
Vomiting	9.1	5.0	8.6	8.0	2.2
<b>General Disorders and Administration Site Conditions</b>					
Asthenia	2.2	0.7	2.2	2.7	0
Chest pain	6.1	1.4	0	2.7	0
Feeling abnormal	3.0	0	0	0	0
Infusion site pain or burning	0	5.8	0	0	0
Injection site extravasation	0	2.2	0	0	0
Peripheral edema	2.6	7.2	5.0	5.3	10.9
Pyrexia	3.0	0.7	0.7	1.3	0
<b>Infections and Infestations</b>					
Nasopharyngitis, Sinusitis, Upper respiratory tract infections, Pharyngitis	2.6	2.2	4.3	16.0	4.3
<b>Injury, Poisoning and Procedural Complications</b>					
Graft complication	9.5	1.4	0	0	0
<b>Metabolism and Nutrition Disorders</b>					
Fluid overload	3.0	1.4	0.7	1.3	0
Gout	0	2.9	1.4	0	0
Hyperglycemia	0	2.9	0	0	2.2
Hypoglycemia	0.4	0.7	0.7	4.0	0
<b>Musculoskeletal and Connective Tissue Disorders</b>					
Arthralgia	3.5	1.4	2.2	4.0	4.3
Back pain	2.2	2.2	3.6	1.3	4.3
Muscle cramp	29.4	0.7	0.7	2.7	0
Myalgia	0	3.6	0	1.3	0
Pain in extremity	5.6	4.3	0	2.7	6.5
<b>Nervous System Disorders</b>					
Dizziness	6.5	6.5	1.4	1.3	4.3
Headache	12.6	2.9	0.7	4.0	0
<b>Respiratory, Thoracic and Mediastinal Disorders</b>					
Cough	3.0	2.2	0.7	1.3	0
Dyspnea	3.5	5.8	1.4	1.3	2.2
Nasal congestion	0	1.4	2.2	1.3	0
<b>Skin and Subcutaneous Tissue Disorders</b>					
Pruritus	3.9	2.2	4.3	2.7	0
<b>Vascular Disorders</b>					
Hypertension	6.5	6.5	4.3	8.0	6.5
Hypotension	39.4	2.2	0.7	2.7	2.2

\* EPO=Erythropoietin

One hundred thirty (11%) of the 1,151 patients evaluated in the 4 U.S. trials in HDD-CKD patients (studies A, B and the two post marketing studies) had prior other intravenous iron therapy and were reported to be intolerant (defined as precluding further use of that iron product). When these patients were treated with Venofer there were no occurrences of adverse reactions that precluded further use of Venofer [see *Warnings and Precautions* (5)].

